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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/591,899

09/07/2006

Masanori Somei

1254-0323PUS1

7982

2292 7590 11/28/2008
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EXAMINER

PAGONAKIS, ANNA

ART UNIT

PAPER NUMBER

1614

NOTIFICATION DATE

DELIVERY MODE

11/28/2008

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No. 10/591,899	Applicant(s) SOMEI ET AL.	
	Examiner ANNA PAGONAKIS	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 August 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 4-12 is/are pending in the application.
- 4a) Of the above claim(s) 6-12 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 4 and 5 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>See Continuation Sheet</u> . | 6) <input type="checkbox"/> Other: _____ |

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :6 sheets, 12/7/2006; 3 sheets, 9/7/2006.

DETAILED ACTION

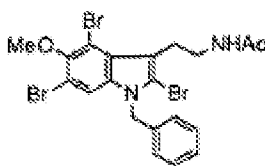
Applicant's election with traverse of the specie election in the reply filed on 8/25/2008 is acknowledged. The traversal is on the ground(s) that Groups I-III form a single general inventive concept under PCT Rule 13.1. This is not found persuasive because as stated in the restriction requirement mailed on 7/25/2008, the inventions listed as Groups I-III lack the same special technical feature because Group I is directed to a compound, Group II to a pharmaceutical and Group II to a method of treatment.

The requirement is still deemed proper and is therefore made FINAL.

Claims 4-12 are pending in the application. Claims 6-12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected subject matter, there being no allowable generic or linking claim. Accordingly, claim 6 is amended and claims 7-12 are newly added.

Expansion of Election of Species Requirement

A reasonable and comprehensive search conducted by the Examiner determined that the prior art at the time of the present invention was such that it did not anticipate or render obvious the elected specie of:



In light of this discovery, the search was expanded to the following compound: 2-bromomelatonin.

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The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

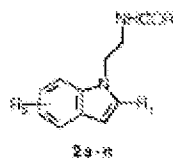
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary.

Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 4-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tarzia et al (Journal of Medicinal Chemistry, 40, 2003-2010, 1997).

Tarzia et al teach 2-bromomelatonin (compound 2b):



compd	R	E ₁	E ₂	IC ₅₀	K _i	relative affinity ^b	GTPγS index ^c	cAMP index ^d	activity ^e
aMT (1)				2.2	0.61	1	1	1	A
2a	CH ₃	H	6-OCH ₃	12	3.4	5.45	0.85	0.85	A
2b	CH ₂ CH ₃	Br	6-OCH ₃	0.16	0.044	0.073	1.3	1.2	A
2c	CH ₂ CH ₃	phenyl	6-OCH ₃	0.052	0.014	0.024	1.45	1.15	A
2d	CH ₂ CH ₃	COOCH ₃	6-OCH ₃	0.83	0.23	0.38	0.93	1.02	A
2e	CH ₂ CH ₃	phenyl	H	82	23	38	0.95	0.98	A
2f	CH ₂ CH ₃	H	5-OCH ₃	5400	1500	2450	0.29	0.4	PA
2g	CH ₂ CH ₃	I	5-OCH ₃	360	90	165	0.75	0.8	A--PA
2h	cyclopropyl	H	H	3200	880	1450	0.14	0.2	AN--PA
2i	cyclobutyl	H	H	18000	5000	8180	0.16	0.25	AN--PA
2j	cyclobutyl	phenyl	H	10000	2800	4550	0.18	0.25	AN--PA
2k	CF ₃	H	6-OCH ₃	35	9.6	16	0.97	0.99	A
2l	cyclopropyl	H	6-OCH ₃	89	24	40	0.32	0.44	PA
2m	CH ₂ CH ₂ CH ₃	H	6-OCH ₃	11	3.0	5	1.1	1	A
2n	CH ₂ CH ₃	H	6-OCH ₃	7.1	1.9	3.2	0.98	0.96	A
6				4.8	1.3	2.2	1.05	1.06	A
7				7100	1900	3230	0.08	0	AN
2-Br-melatonin				0.13	0.036	0.059	1.02	1.15	A
2-Ph-melatonin				0.062	0.017	0.028	0.82	0.78	A--PA
6-Cl-melatonin				3.6	0.99	1.6	0.91	1.04	A

^a IC₅₀ and K_i values are expressed in nM and are the means of three to 20 independent determinations, derived from nonlinear fitting strategies. The SEM values were below 15% of the mean. ^b Relative affinity = (IC₅₀ compound/IC₅₀ aMT) determined in parallel, in the same experiment. ^c GTPγS index = [(IC₅₀ with GTPγS)/(IC₅₀ without GTPγS)] compound/[(IC₅₀ with GTPγS)/(IC₅₀ without GTPγS)] aMT. ^d cAMP index = (percent inhibition compound)/(percent inhibition aMT) determined in parallel in the same experiment. ^e A, agonist; PA, partial agonist; AN, antagonist.

Claims 4-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Naguib et al (Anesth Analg, 2003, 97: 763-8).

Naguib et al teach that 2-bromomelatonin was synthesized by reacting melatonin with phenyltrimethylammonium tribromide in tetrahydrofuran (page 763, column 2).

The use of pharmaceutically acceptable salts of 2-bromomelatonin would have been a matter well within the purview of the skilled artisan. As taught by Remington's Pharmaceutical Sciences, drugs may be formulated into salts to modify the duration of action of a drug; to modify the transportation and distribution of the drug in the body; to reduce toxicity; and to overcome difficulties encountered in pharmaceutical formulation procedures or in the dosage form itself (see column 2 of page 424, first paragraph). Thus, it would have been obvious to the skilled artisan motivated by any one or more of these factors to formulate the active agent 2-bromomelatonin into a pharmaceutically acceptable salt to enhance

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the pharmacokinetic parameters of the drug or to reduce the toxicity with the reasonable expectation that the therapeutic benefit of the agent in salt form would have been the same or substantially similar to that of the agent itself.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNA PAGONAKIS whose telephone number is (571)270-3505. The examiner can normally be reached on Monday thru Thursday, 9am to 5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Patricia A. Duffy/
Primary Examiner, Art Unit 1645

AP